

## **REMARKS**

### **Amendments**

The formulas in claims 1 and 27 are amended to indicate that the group -O is -OH. Support for this amendment can be found throughout the specification. See, for example, the structural depictions of compounds III and IV at page 44 and their compound names presented at pages 45 and 46. See also the structural depictions compounds VII and VIII at page 47 and their compound names presented at pages 48 and 49. See also, for example, the structural depictions of compounds I and V at pages 44 and 47, respectfully, and their respective compound names presented at pages 43 and 47, respectively. Other examples of using -O to represent -OH in the structural formulas can be found throughout the examples.

Claims 1 and 27 are also amended to refer to salts, esters and salts of esters thereof. See, e.g., page 26, lines 20-22. Claims 18 and 36 are cancelled. Compare claims 16 and 34 in which the partial structures depicted therein for G2 result, are in each case, in guanidinyI.

Claim 3 is amended to correct an obvious typographical error. Claims 42 and 43 are cancelled. Claim 58 is amended to delete the statement of intended use and to recite that the composition further comprises a pharmaceutically acceptable carrier, diluent or adjuvant. See, e.g., page 41, lines 33-35. Claims 59-73 directed to pharmaceutical compositions, which recited specific statements of intended use are cancelled. Claim 74 is amended to delete the statement of intended use and claim 75 is amended to depend from claim 74.

New claim 76 is directed to specific compounds. See, e.g., the list compounds presented at pages 20-24 and the compounds presented in the examples. New claims 77-93 are claims directed to pharmaceutical compositions and methods of use of the compounds recited in claim 76. These new claims are supported throughout the disclosure and the original claims.

### **Objection**

Contrary to the assertion in the Office Action, the disclosure provides more than adequate support for the amendments previously presented and those presented herein. See the discussion below regarding the rejections under 35 USC §112. For the reasons discussed below, withdrawal of the objection is respectfully requested.

**Rejections under 35 USC §112, first and second paragraph**

Claims 1-16, 18-19, 22-34, 36-37 and 40-75 are rejected under 35 USC §112, first paragraph, on grounds of alleged lack of enablement and lack of written description, and also under 35 USC §112, second paragraph. These rejections are respectively traversed.

In the Office Action, the Examiner rejects the claims on grounds of allegedly failing to satisfy the “how to make” requirement and on grounds of alleged indefiniteness, on the basis of “dangling valencies” for the oxygen atoms at the end of the molecule. This rejection is overcome by the amendment to the formulas in claims 1 and 27 wherein -O is replaced by -OH. Further, one of ordinary skill in the art upon reading Applicants’ specification would recognize that -O depicted in the structural formulas is intended to represent the hydroxyl group -OH. See, for example, the structural depictions of compounds I-IV presented at page 44 of Applicants’ specification. Comparing these structural formulas with the names provided for the represented compounds, one of ordinary skill in the art would clearly recognize that the -O at the end of the structural formula is intended to indicate the hydroxyl portion of the terminal carboxylic acid group. See also, for example, the structural depiction of compounds V, VII, VIII, X, XI, XII, XXVII, and XXX and their respective compound names as presented in Applicants’ specification.

In light of the above discussion, it is respectfully submitted that the disclosure as filed reasonably conveys possession of the claimed subject matter. See, e.g., *In re Kaslow*, 217 USPQ 1089 (Fed. Cir. 1982). *Ipsis verbis* disclosure is not required. See, e.g., *Fujikawa v. Wattanasin*, 39 USPQ 1895 (Fed. Cir. 1996).

According to the indefiniteness rejection presented at pages 8-9 of the Office Action, it is noted that firstly the Examiner asserts the definitions of A<sub>3</sub>, A<sub>4</sub> and X as presented in the claims lacks sufficient antecedent basis in the specification or the originally filed claims. An assertion of lack of antecedent basis in the specification or original claim does not present a rational as to why the language of the claims would be indefinite. One of ordinary skill in the art upon reading the claims, in particular, the definitions of A<sub>3</sub>, A<sub>4</sub>, and X, would clearly understand the scope of the claims.

The assertion of lack of antecedent basis in the specification and the original claim is not an issue of indefiniteness under § 112, second paragraph, but instead an issue of written description under § 112, first paragraph. The issue of the written description is discussed

below.

Also, X in claims 1 and 27 is defined as O or S. See original claims 1 and 27 and the specification, for example, page 5, line 22.

It is also asserted that in claims 1 and 27 when A<sub>3</sub> is NH and A<sub>4</sub> is NH<sub>2</sub>, the resultant moiety is N=NH-NH<sub>2</sub>. This is incorrect. When A<sub>3</sub> is NH and A<sub>4</sub> is NH<sub>2</sub>, then G<sub>2</sub> is the moiety -C(NH)-NH<sub>2</sub>, and -NH-G<sub>2</sub> is guanidinyll.

As noted above, claims 18 and 36 are cancelled. However, there is more than sufficient antecedent basis for the claimed subject matter. As noted above, NH - G<sub>2</sub> forms guanidinyll when A<sub>3</sub> is NH and A<sub>4</sub> is NH<sub>2</sub>.

With regards to written description, the Examiner asserts that there is no descriptive support in the specification for the definitions of A<sub>3</sub>, A<sub>4</sub>, NH-G<sub>2</sub> and X, specifically wherein A<sub>3</sub> is NH, A<sub>4</sub> is NH<sub>2</sub>, -N-G<sub>2</sub> is -NH-G<sub>2</sub>, and X is -NH.

Firstly, it is noted that X is defined as O or S in the claims, not NH.

While the Examiner agrees that *ipsis verbis* disclosure is not required for the above definitions, the Examiner still maintains that there is insufficient description for the claimed subject matter.

One of ordinary skill in the art, upon reading Applicants' original claim 1, would recognize that groups A<sub>1</sub> and A<sub>2</sub> are divalent structures. Thus, upon reading the claim, one of ordinary skill in the art would refer to the specification to see what structure was intended when A<sub>1</sub> or A<sub>2</sub> was "N." Similarly, one of ordinary skill in the art would recognize that A<sub>3</sub> is a monovalent or divalent structure (depending on the partial structural formula selected) and again would refer to the specification to see what was intended when A<sub>3</sub> was "N." Also, one of ordinary skill in the art would recognize that A<sub>4</sub> is a monovalent structure and, again, would look to the specification to see what was intended when A<sub>4</sub> was "N." In addition, upon seeing the substructures -N- and -O in the formula within the claim, one of ordinary skill in the art would refer to the specification to see what is intended by these structural depictions.

Throughout the specification, and particularly the examples, support can be found for the claim definitions of A<sub>3</sub>, A<sub>4</sub> and -NH-G<sub>2</sub> in the compounds and of intermediates thereof. In reviewing the structural formulas and their corresponding compound names, one of ordinary skill in the art would recognize that whenever A<sub>1</sub> or A<sub>2</sub> is a moiety containing "N" that moiety is NH. See, e.g., the structural formulas of compounds II-V, VI-VIII and X-XII

and their corresponding compound names.

With respect to A<sub>3</sub> and A<sub>4</sub>, see, for example, reaction scheme C at page 31 wherein the final compound C-9 exhibits a H<sub>2</sub>N-C(=NH)-NH- group for the structure G<sub>2</sub>-NH-G<sub>1</sub>. See also the structural depiction of Compound IV at page 44 (which shows N atoms with unfulfilled valencies) and the name of Compound IV at page 21 and 46, i.e., 2-Benzenesulfonylamino-3-{{5-(3-guanidino-propylcarbamoyl)-thiophene-2-carbonyl]-amino}-propionic acid, trifluoroacetic acid salt, which clearly indicates that the unfulfilled valencies are in fact fulfilled by H atoms.

Compare also Compound VIII depicted at page 21 and page 47 and the name of Compound VIII at page 21 and page 49, 3-{{5-(3-guanidino-propylcarbamoyl)-thiophene-2-carbonyl]-amino}-3-phenyl-propionic acid. See also Compound XIX depicted at page 54 which exhibits a H<sub>2</sub>N-C(=NH)-NH- group for the structure G<sub>2</sub>-NH-G<sub>1</sub>. See also Compound XXI depicted at page 59 which exhibits a H<sub>2</sub>N-C(=NH)-NH- group for the structure G<sub>2</sub>-NH-G<sub>1</sub>. Compare also Compound XXXI depicted at page 63 and the name of compound XXX at page 23 and page 65, 3-{{5-(2-guanidino-ethylcarbamoyl)-thiophene-2-carbonyl]-amino}-2-(pyrimidin-2-ylamino)-propionic acid bis trifluoroacetic acid salt. See also the description of urea and guanidino at page 25, and original claims 18, 19, 37 and 38 which recite that -NH-G<sub>2</sub> forms a urea containing moiety or a guanidino containing moiety.

Similarly, comparing the structural formulas depicted in the specification in their corresponding compound names, one of ordinary skill in the art would recognize that whenever structural formula contains the depicted structures of -N-, -O-, or -N, these structures, as clearly indicated by the corresponding compound names, are intended to represent -NH-, -OH, and -NH<sub>2</sub>, respectively. See, e.g., compounds I-VIII.

The Examiner's comments concerning the court's rationale in *In re Fujikawa v. Wattanasin*, 39 USPQ 1895 (Fed. Cir. 1996) are irrelevant to the present issue. The portion of the opinion quoted by the Examiner concerns an argument that *ipsis verbis* disclosure was actually present, not an argument that support was present despite no *ipsis verbis* description.

In *Fujikawa*, the question was whether Wattanasin's application provided adequate description of a particular subgenus. The Board held that the application did not provide adequate direction with respect to the subgenus, since the proposed subgenus did not contain Wattanasin preferred compounds and there were no blaze marks as to what compounds other

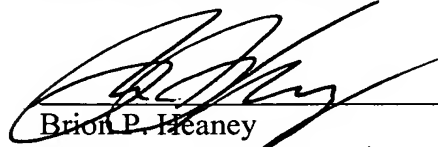
than the preferred compounds might be of interest.

Fujikawa argued that the proposed count was in fact disclosed *ipsis verbis* in Wattanasin's application. In making this argument, Fujikawa asserted that with regards to one of the variables in the proposed subgenus, i.e., variable R, Wattanasin disclosed cyclopropyl as a possible R moiety. However, the court held that, merely because cyclopropyl was listed as a possibility for the R moiety, this did not mean that there was *ipsis verbis* support for all of the species encompassed within the genus of Wattanasin in which R was cyclopropyl. This is the portion of the decision which is quoted in the Office Action. As noted above, this portion of the decision deals with an argument based on *ipsis verbis* support, not an argument that written description was present based on non *ipsis verbis* support.

In the instant case, one of ordinary skill in the art upon reading the original claims and looking back to the specification and the compounds described therein, would find support for the descriptions are cited in the present claims. Moreover, the compounds set forth in the examples clearly define blaze marks to lead one of ordinary skill in the art to the definitions recited in Applicants' claims. In view of the above, it is respectfully that more than adequate description is provided by Applicants' disclosure to reasonable convey that Applicants' had procession of the claimed subject at the time of filing.

In view of the above remarks, it is respectfully that applicants' disclosure satisfies the requirements under 35 USC 112, first and second paragraphs. Withdrawal of the rejections is respectfully requested.

Respectfully submitted,



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